

REMARKS-General

Applicant has rewritten all claims to define the invention more particularly and distinctly so as to overcome the technical rejections and define the novelty of the invention over the prior art.

The Objection to The Claims Rejection Under 35 U.S.C. 112

The Office Action stated that the Markush language "selected from the group consisting of" followed by "but is not limited to" is deemed improper under 35 U.S.C. 11,2 second paragraph. The new Claims 9 to 13 have been amended to better define patentability.

The Objection to The Claims Rejection Under 35 U.S.C. 103

The Office Action maintained the rejection of Claims 4-8 as being unpatentable over Sato et al and in view of Remington's Pharmaceutical Sciences' discussion of the uses of alcohol and acetone as solvents. Amendment A stated that improved antibiotic activity was found when mixing fluoroquinolone antibiotics and alcohol and acetone. The Office Action argues that in the absence of a comparative showing, the rejection is maintained under 35 U.S.C. 103.

The prior art does not teach a composition comprising a fluoroquinolone antibiotic combined with alcohol and acetone for the treatment of bacterial infections of the skin caused by susceptible organisms.

As described in Goodman and Gillman, the fluoroquinolone antibiotics are bactericidal against multiple aerobic bacteria. However, many anaerobic bacteria are resistant. In addition, resistance to these drugs even by aerobic bacteria may develop during therapy. The mechanism of action of fluoroquinolone antibiotics is by inhibition of eukaryotic type II topoisomerase enzyme. Alcohol and acetone are directly bactericidal, causing bacterial cell death on chemical contact by causing damage to proteins, nucleic acids or cell membrane lipids, resulting in altered permeability of the bacterial cell membrane. This process is in contrast to the enzymatic inhibitory process of the fluoroquinolones.

Consistent with the present invention, it has been found that a combination on the skin of a fluoroquinolone antibiotic mixed with alcohol and acetone exert a clinically significant synergistic effect. Fluoroquinolones exert their antimicrobial effect by interference with the intracellular enzyme DNA gyrase which is needed for synthesis of bacterial DNA. Alcohol and acetone exert cytologic damage by altering cell membranes. The altered permeability allows for easier cellular access of fluoroquinolone antibiotics, thus synergistically facilitating their enzymatic interference.

Therefore, the bactericidal spectrum of activity of this invention includes both anaerobic and aerobic bacteria. As such, a composition consisting of a fluoroquinolone antibiotic mixed with alcohol and acetone allows for a preparation which overcomes the limitation of activity of the fluoroquinolones as well as any emergent resistance of bacteria to fluoroquinolones. In addition, alcohol and acetone have the limitation of volatility and non-penetrability into the stratum corneum of the skin. This is not the case with the

fluoroquinolones. Consequently, the fluoroquinolones are a vital part of the composition, necessary to overcome the limitations of the alcohol and acetone.

The result of combining the three agents for their respective antibacterial activity produces a highly effective and unique preparation for patients.

The Office Action listed Grohe, U.S. Patent 4,844,902, to cite the state of the art with respect to topically applicable preparations of fluoroquinolone type antibiotics. Grohe has combined two known ingredients for therapy of the oral cavity. This combination is similar to the Applicant's invention in that two ingredients, known to someone versed in the art, were combined in a unique combination.

As requested by the Office Action, a copy of the Information Disclosure Statement of February 27, 1998, has been enclosed.

As requested by the Office Action, the contact phone number for the Applicant is 310-550-7661.

Conclusion

For all the reasons given above, the applicant respectfully submits that the errors in the Claims comply with Section 112 and the Claims define over the prior art under Section 103 because the Applicant has shown that the fluoroquinolone and alcohol and acetone mixture are a unique synergistic topical combination. Accordingly, Applicant submits

that this application is now in full condition for allowance, which action Applicant respectfully solicits.

Conditional Request for Constructive Assistance

Applicant has amended the Claims of this application so that they are proper, definite, and define novel structure which is also unobvious. If, for any reason this application is not to be believed in full condition for allowance, Applicant respectfully requests the constructive assistance and suggestions of the Examiner pursuant to MPEP 706.03(d) and 707.07(j) in order that the undersigned can place this application in allowable condition as soon as possible and without the need for further proceedings.

Very respectfully,

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Certificate of Mailing: I certify that on the date below this document and referenced attachments, if any, will be deposited with the U.S. Postal Service as certified mail in an envelope addressed to: "ATTN: P. Spivak, GAU 1614, Box Non-Fee Amendments, Assistant Commissioner for Patents, Washington DC 20231."

1999 April 28

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Letantia Bussell, Applicant